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10/734,563	12/12/2003	Joseph A. Sorge	25436/2345C	2401

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EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
05/20/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/734,563	**Applicant(s)** SORGE ET AL.	
	Examiner Richard G. Hutson	**Art Unit** 1652	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 28 April 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-10 and 12-21*.
   Claim(s) withdrawn from consideration: *11 and 22-26*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Richard G Hutson, Ph.D./
Primary Examiner, Art Unit 1652

Continuation of 11. does NOT place the application in condition for allowance because: Claims 1-10 and 12-21 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection was stated in the previous offices action as it applied to Claims 1-10 and 12-21. In response to this rejection applicants have amended claims 1-7 and traverse the rejection as it applies to the newly amended claims.
Applicants continue to submit that the specification discloses several mutant DNA polymerases having different mutations at V93 as well as several working examples using different Archael DNA polymerases.
Applicants continue to submit that in order to meet the written description requirement, applicants need only describe the claimed invention in a manner such that one of skill in the art would understand that at the time of filing, applicant was in possession of the invention as claimed. Applicants continue to submit that applicants have met this initial requirement, in that applicant's specification provides the sequences for a range of archaeal DNA polymerases showing where to mutate to achieve the desired reduction in base analog detection activity and that the office has not set forth express findings of fact to support the lack of written description.
Applicants question what is it about the recited DNA polymerase that is not adequately described. Applicants question if it is the mutation at V93, in one of the recited exonuclease motifs or something else.
As has been previously stated, it is the breadth of the claimed genus versus the disclosed species and the knowledge in the specific art that lies at the core of the claims identified issues. Applicants continued description of the taught species as well as applicants discussion of supposed limitations of the claimed genus continue to be acknowledged, however, are not persuasive in describing the breadth of the claimed genus that reads on any DNA polymerase comprising at least one amino acid mutation in a exoI, II, or III motif. Applicants statements that the claims contain "characteristics" which are they are directed to an Archael DNA polymerase comprising certain mutations continues to be acknowledged, however, given applicants use of the terminology "at least one amino acid mutation…" in the claim, not found persuasive. This language effectively eliminates applicant's recited "characteristics" thus opening up the claimed genus. Thus the predictable structure for the recited function for the encompassed polymerases of the claimed genus is insufficient.
Similarly the representative species are not sufficient in describing the breadth of the claimed genus.
The evidence and reasoning to support this rejection is as was originally presented to applicants.
As previously stated, the specification fails to describe additional representative species of these mutant DNA polymerases by any identifying structural characteristics or properties other than the activities recited in the claims, for which no predictability of structure is apparent. While applicants argue that they do describe characteristics of the claimed genus, these "characteristics" are not limitations of the breadth of the claimed genus. Thus, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention.
Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-10 and 12-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a Pfu DNA polymerase comprising the amino acid sequence of SEQ ID NO: 89 with a single amino acid substitution at position V93, does not reasonably provide enablement for any possible archael DNA polymerases and compositions and kits comprising said archael DNA polymerase, wherein said mutant is a Pfu DNA polymerase (SEQ ID NO: 89) further comprising at least one amino acid mutation in an exoI, exo II or exo III motif and another amino acid mutation at position V93 of the polymerase, wherein said polymerase is deficient in 3'-5' exonuclease activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.
This rejection was stated in the previous office action as it applied to Claims 1-10 and 12-21. In response to this rejection applicants have amended claims 1-7 and traverse the rejection as it applies to the newly amended claims.
Applicants continue to submit that applicants specification coupled with the knowledge in the art provides substantial guidance as to the specific, conserved motifs within Archael DNA polymerases that are associated with the 3'-5' exonuclease activity of the polymerase. Applicants submit those domains associated with such activity and that contrary to the previous office action, applicant's specification in combination with the art provides a known correlation between structure and function.
Applicants continue to submit that the other Wands factors also weigh in favor of enablement. Applicants submit that the level of skill in the art was high, and applicant's specification discloses several working examples. Applicants further submit that applicants provide detailed information on site-directed mutagenesis necessary to generate the necessary mutants.
Applicant's complete argument continues to be acknowledged, however, not found persuasive for the reasons previously presented and repeated herein and above.
It continues that the breadth of the claimed genus is so large that applicants have not sufficiently enabled the scope of the claimed genus. As above applicants comments regarding "characteristics" of the claimed genus are acknowledged, however, it continues that these characteristics are not descriptive of the breadth of the claimed genus. Much of the problems with the current rejection stems from the same issue as above, the breadth of the claimed genus that stems from applicants use of the terminology "DNA polymerase comprising at least one amino acid mutation in the ….".
While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without effecting deficiencies in 3'-5' exonuclease activity; (B) the general tolerance of Family B/pol I-type and pol II-type DNA polymerases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of any DNA polymerase including both Family B/pol I-type and pol II-type DNA polymerases with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to reduce the base analog detection activity claimed and the fact that the relationship between

the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those mutant DNA polymerases of the claimed genus having the claimed activities.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any mutant archael DNA polymerase with a reduced base analog detection activity. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those mutant DNA polymerases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1-10 and 12-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-5, 13, 15, 17-29, 31-42, 58-66 of copending Application No. 10/298,680. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims of both applications are drawn to an Archael DNA polymerase comprising an amino acid sequence of SEQ ID NO: 89, further comprising at least one amino acid mutation in an exoI, II, or III motif and another mutation at V93, wherein said DNA polymerase is deficient in 3'-5' exonuclease activity.
This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.
Applicants request that this provisional rejection be held in abeyance until that time in which one of the two patent applications in question is deemed in condition for allowance, Is acknowledged..